REMARKS

Claims 25-31, 37, 38, and 42-72 are pending after entry of this Response and Preliminary Amendment. Claims 1-24, 32-36, and 39-41 have been canceled without prejudice. Claims 25-28, 31, 37, and 38 have been amended. Claims 42-72 have been added. Claims 25 and 37 are the only independent claims.

No additional fee is believed due. No extension of time fee is believed due because this Response and Preliminary Amendment is timely filed by August 5, 2002 (August 3 and 4, 2002 being Saturday and Sunday). No additional claim fee is believed due because 32 claims have been canceled and 31 dependent claims have been added. However, in the event a fee is due, please charge it to Deposit Account No. 50-1017 (**Billing No. 210147.0039/16U1**).

For the Examiner's convenience, the Applicants have enclosed a "**Clean Copy of Claims, as Amended in the Response to Restriction Requirement and Preliminary Amendment**," in which all claims pending after entry of this Response and Preliminary Amendment are listed in an order which the Applicants believe is appropriate for issue.

Support in the Specification

The title has been amended in view of the Restriction Requirement.

The Amendments to claims 25 and 37 merely remove non-elected subject matter from those claims.

The Amendment to claim 26 and addition of claims 57-64 simply distributes the nine elements that were previously recited in Markush format in claim 26 into nine single-element dependent claims.

The Amendment to claim 27 is simpiy a grammatical improvement.

The Amendment to claim 28 and addition of claims 42-44simply distributes the four elements that were previously recited in Markush format in claim 28 into four single-element dependent claims.

The Amendment to claim 31 and addition of claims 45 and 46 simply distributes the three elements that were previously recited in Markush format in claim 31 into three single-element dependent claims.

The Amendment to claim 38 and addition of claims 65-72 simply distributes the nine elements that were previously recited in Markush format in claim 38 into nine single-element dependent claims.

Addition of claims 47-56 (each of which depends from claim 37) simply parallels the recitations of dependent claims 27, 28, 42-44, 29-31, 45, and 46, respectively (each of which depends from claim 25).

For the foregoing reasons, the Applicants respectfully contend that the amendments and additions made herein do not include new matter.

Summary

The Applicants respectfully contend that each of pending claims 25-31, 37, 38, and 42-72 corresponds to the elected Group, and that each is in condition for allowance. An early and favorable office action on the merits is requested.

Respectfully submitted,
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2 August 2002 By: _____
(Date)

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Enclosures

Marked-Up Copy of Claims Amended in the Response to Restriction Requirement and Preliminary Amendment

25. (Amended) A method of determining whether a test composition is useful for alleviating a bone-related disorder, the method ~~selected from the group consisting of~~ comprising:

~~a)~~

maintaining a cell which comprises a biologically active MRR protein in the presence of the test composition and

comparing i) an activity of the MRR protein of the cell maintained in the presence of the test composition and

ii) the same activity of the MRR protein of a cell of the same type maintained in the absence of the test composition,

wherein a difference between

i) an activity of the MRR protein of the cell maintained in the presence of the test composition and

ii) the same activity of the MRR protein of the cell of the same type maintained in the absence of the test composition

is an indication that the test composition is useful for alleviating a bone-related disorder~~;~~

~~b) maintaining a cell which comprises a biologically active MRR protein in the presence of the test composition and~~

~~comparing i) the level of expression of the mrr gene in the cell maintained in the presence of the test composition and~~

~~ii) the level of expression of the mrr gene in the MRR protein of a cell of the same type maintained in the absence of the test composition,~~

~~wherein a difference between~~

~~i) the level of expression of the mrr gene in the cell maintained in the presence of the test composition and~~

~~ii) the level of expression of the mrr gene in the MRR protein of a cell of the same type maintained in the absence of the test composition~~

~~is an indication that the test composition is useful for alleviating a bone-related disorder;~~

~~c) maintaining a cell which comprises a biologically active MRR protein in the presence of the test composition and~~

~~comparing -- i) a bone phenotype of the cell maintained in the presence of the test composition and~~

~~ii) the same bone phenotype of a cell of the same type maintained in the absence of the test composition,~~

~~wherein a difference between~~

~~i) the bone phenotype of the cell maintained in the presence of the test composition and~~

~~ii) the same bone phenotype of the cell maintained in the absence of the test composition~~

~~is an indication that the test composition is useful for alleviating a bone-related disorder;~~

~~d) administering the test composition to a first animal which naturally harbors an mrr gene and~~

~~comparing i) a bone phenotype of the first transgenic animal and~~

~~ii) the same bone phenotype of a second animal which naturally harbors an mrr gene and to which the test composition is not administered.~~

~~wherein a difference between~~

~~i) the bone phenotype of the first animal and~~

~~ii) the same bone phenotype of the second animal~~

~~is an indication that the test composition is useful for alleviating a bone-related disorder;~~

~~e) administering the test composition to a first non-human transgenic animal which harbors an exogenous mrr gene and~~

~~comparing i) a bone phenotype of the first transgenic animal and~~

~~ii) the same bone phenotype of a second non-human transgenic animal which harbors an exogenous mrr gene and to which the test composition is not administered,~~

~~wherein a difference between~~

~~i) the bone phenotype of the first transgenic animal and~~

~~ii) the same bone phenotype of the second transgenic animal~~

~~is an indication that the test composition is useful for alleviating a bone-related disorder; and~~

~~f) maintaining an artificial membrane which comprises a biologically active MRR protein in the presence of the test composition and~~

~~comparing i) an activity of the MRR protein of the artificial membrane maintained in the presence of the test composition and~~

~~ii) the same activity of the MRR protein of an artificial membrane of the same type maintained in the absence of the test composition,~~

~~wherein a difference between~~

~~i) the activity of the MRR protein of the artificial membrane maintained in the presence of the test composition and~~

~~ii) the same activity of the MRR protein of artificial membrane of the same type maintained in the absence of the test composition~~

~~is an indication that the test composition is useful for alleviating a bone-related disorder~~.

26. (Amended) The method of claim 25, wherein the bone-related disorder is ~~selected from the group consisting of~~ osteoporosis~~, Paget's disease, hyperthyroidism, hyperparathyroidism, osteomalacia, chronic renal failure, Cushing's syndrome, an osteogenic cancer, and a non-osteogenic cancer that has metastasized to bone tissue~~.

27. (Amended) The method of claim 25, wherein the biologically active MRR protein ~~is a protein having~~ has the amino acid sequence SEQ ID NO: 1.

28. (Amended) The method of claim 25, wherein the activity ~~of the MRR protein~~ is ~~selected from the group consisting of~~ a proteolytic activity~~, a pore modulating activity, an enzyme modulating activity, and a gene transcription modulating activity~~.

31. (Amended) The method of claim 30, wherein the ~~animal~~ cell is ~~selected from the group consisting of~~ a human cell~~, a mouse cell, and a rat cell~~.

37. (Amended) A method of determining the propensity of a test compound to induce a bone-related disorder in a human patient, the method ~~selected from the group consisting of~~ comprising:

~~a)~~

maintaining a cell which comprises a biologically active MRR protein in the presence of the test composition and

comparing i) an activity of the MRR protein of the cell maintained in the presence of the test composition and

ii) the same activity of the MRR protein of a cell of the same type maintained in the absence of the test composition,

wherein a difference between

i) an activity of the MRR protein of the cell maintained in the presence of the test composition and

ii) the same activity of the MRR protein of the cell of the same type maintained in the absence of the test composition

is an indication that the test composition is likely to induce the bone-related disorder in a human patient;

~~b) maintaining a cell which comprises a biologically active MRR protein in the presence of the test composition and~~

~~comparing i) the level of expression of the mrr gene in the cell maintained in the presence of the test composition and~~

~~ii) the level of expression of the mrr gene in the MRR protein of a cell of the same type maintained in the absence of the test composition,~~

~~wherein a difference between~~

~~i) the level of expression of the mrr gene in the cell maintained in the presence of the test composition and~~

~~ii) the level of expression of the mrr gene in the MRR protein of a cell of the same type maintained in the absence of the test composition~~

~~is an indication that the test composition is likely to induce the bone-related disorder in a human patient;~~

~~c) maintaining a cell which comprises a biologically active MRR protein in the presence of the test composition and~~

~~comparing i) a bone phenotype of the cell maintained in the presence of the test composition and~~

~~ii) the same bone phenotype of a cell of the same type maintained in the absence of the test composition,~~

~~wherein a difference between~~

~~i) the bone phenotype of the cell maintained in the presence of the test composition and~~

~~ii) the same bone phenotype of the cell maintained in the absence of the test composition~~

~~is an indication that the test composition is likely to induce the bone-related disorder in a human patient;~~

~~d) administering the test composition to a first animal which naturally harbors an mrr gene and~~

~~comparing i) a bone phenotype of the first transgenic animal and~~

~~ii) the same bone phenotype of a second animal which naturally harbors an mrr gene and to which the test composition is not administered,~~

~~wherein a difference between~~

~~i) the bone phenotype of the first animal and~~

~~ii) the same bone phenotype of the second animal~~

~~is an indication that the test composition is likely to induce the bone-related disorder in a human patient;~~

~~e) administering the test composition to a first non-human transgenic animal which harbors an exogenous mrr gene and~~

~~comparing i) a bone phenotype of the first transgenic animal and~~

~~ii) the same bone phenotype of a second non-human transgenic animal which harbors an exogenous mrr gene and to which the test composition is not administered,~~

~~wherein a difference between~~

~~i) the bone phenotype of the first transgenic animal and~~

~~ii) the same bone phenotype of the second transgenic animal~~

~~is an indication that the test composition is likely to induce the bone-related disorder in a human patient;~~

~~and~~

~~f) maintaining an artificial membrane which comprises a biologically active MRR protein in the presence of the test composition and~~

~~comparing i) an activity of the MRR protein of the artificial membrane maintained in the presence of the test composition and~~

~~ii) the same activity of the MRR protein of an artificial membrane of the same type maintained in the absence of the test composition,~~

~~wherein a difference between~~

~~i) an activity of the MRR protein of the artificial membrane maintained in the presence of the test composition and~~

~~ii) the same activity of the MRR protein of artificial membrane of the same type maintained in the absence of the test composition~~

~~is an indication that the test composition is likely to induce the bone-related disorder in a human patient~~.

38. (Amended) The method of claim 37, wherein the bone-related disorder is ~~selected from the group consisting of~~ osteoporosis~~, Paget's disease, hyperthyroidism, hyperparathyroidism, osteomalacia, chronic renal failure, Cushing's syndrome, an osteogenic cancer, and a non-osteogenic cancer that has metastasized to bone tissue~~.